wherein n is 0-3 and each X is independently selected from the group consisting of -CN, -CO₂R⁵, -C(O)NR⁵R^{5'}, -C(O)R⁵, -NO₂, -OR⁵, - SR⁵, - NR⁵R^{5'},

-NR 5 C(O)OR 5 , -NR 5 C(O)R 5 , C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₁-C₁₀ alkoxy, C₃-C₁₀ cycloalkyl, C₆-C₁₄ aryl, C₇-C₂₄ alkaryl, C₃-C₁₃ heteroaryl, C₄-C₂₃ alkheteroaryl, substituted C₁-C₁₀ alkyl, substituted C₂-C₁₀ alkenyl, substituted C₁-C₁₀ alkoxy, substituted C₃-C₁₀ cycloalkyl, substituted C₄-C₂₃ alkheteroaryl and -Y-Ar;

wherein if X is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of -CN, $-CO_2R^5$,

-C(O)R⁵, -C(O)NR⁵R^{5'}, -OR⁵, -SR⁵, -NR⁵R^{5'}, -NO₂, -NR⁵C(O)R^{5'}, -NR⁵C(O)OR^{5'} and halogen up to per-halosubstitution;

wherein R^5 and $R^{5'}$ are independently selected from H, C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_3 - C_{10} cycloalkyl, C_6 - C_{14} aryl, C_3 - C_{13} heteroaryl, C_7 - C_{24} alkaryl, C_4 - C_{23} alkheteroaryl, up to per-halosubstituted C_1 - C_{10} alkyl, up to per-halosubstituted C_3 - C_{10} cycloalkyl, up to per-halosubstituted C_2 - C_{10} alkenyl, up to per-halosubstituted C_6 - C_{14} aryl and up to per-halosubstituted C_3 - C_{13} heteroaryl,

wherein Y is -O-, -S-, -N(R⁵)-, -(CH₂)-_m, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R⁵)-, -O(CH₂)_m-, -CHX^a, -NR⁵C(O)NR⁵ R⁵'-, -NR⁵C(O)-, -C(O)NR⁵-, -CX^a₂-, -S-(CH₂)_m- and -N(R⁵)(CH₂)_m-, m = 1-3, and X^a is halogen; and

Ar is a 5-10 member aromatic structure containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur which is unsubstituted or substituted by halogen up to per-halosubstitution and optionally substituted by Z_{n1} ,

wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, $-CO_2R^5$, $-C(O)NR^5R^{5'}$, $-C(O)-NR^5$, $-NO_2$, =O, $-OR^5$, $-SR^5$, $-NR^5R^{5'}$, $-C(O)R^5$, $-SO_2R^5$, $-SO_2NR^5R^{5'}$, $-NR^5C(O)OR^{5'}$, $-NR^5C(O)R^{5'}$, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, C_3-C_{10} cycloalkyl, C_6-C_{14} aryl, C_3-C_{13} heteroaryl, C_7-C_{24} alkaryl, C_4-C_{23} alkheteroaryl, substituted C_1-C_{10} alkyl, substituted C_3-C_{10} cycloalkyl, substituted C_7-C_{24} alkaryl and substituted C_4-C_{23} alkheteroaryl;

wherein if Z is a substituted group, it is substituted by the one or more substituents independently selected from the group consisting of -CN, $-CO_2R^5$, $-C(O)R^5$, $-C(O)NR^5R^5$, $-O(O)NR^5R^5$, $-O(O)NR^5$, -O(O)N

-NR 5 C(O)OR 5 , C $_1$ -C $_{10}$ alkyl, C $_1$ -C $_{10}$ alkoxy, C $_3$ -C $_{10}$ cycloalkyl, C-C $_{10}$ heteroaryl, C $_6$ -C $_{14}$ aryl, C $_4$ -C $_{24}$ alkheteroaryl and C $_7$ -C $_{24}$ alkaryl

A is a heteroaryl moiety selected from the group consisting of

wherein

 R^1 is selected from the group consisting of halogen, C_3 - C_{10} alkyl, C_3 - C_{10} cycloalkyl, C_1 - C_{13} heteroaryl, C_{6^-14} aryl, C_{7^-24} alkaryl, up to per-halosubstituted C_1 - C_{10} alkyl, up to per-halosubstituted C_3 - C_{10} cycloalkyl, up to per-halosubstituted C_1 - C_{13} heteroaryl, up to per-halosubstituted C_{6^-14} aryl, and up to per-halosubstituted C_{7^-24} alkaryl;

 R^2 is selected from the group consisting of H, $-C(O)R^4$, $-CO_2R^4$, $-C(O)NR^3R^{3'}$, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_7-C_{24} alkaryl, C_4-C_{23} alkheteroaryl, substituted C_1-C_{10} alkyl, substituted C_3-C_{10} cycloalkyl, substituted C_7-C_{24} alkaryl and substituted C_4-C_{23} alkheteroaryl,

where R^2 is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of -CN, - CO_2R^4 , -C(O)-NR³R^{3'},

-NO₂, -OR⁴, -SR⁴, and halogen up to per-halosubstitution,

wherein R^3 and $R^{3'}$ are independently selected from the group consisting of H, - OR^4 , - SR^4 , - $NR^4R^{4'}$, - $C(O)R^4$, - CO_2R^4 , - $C(O)NR^4R^{4'}$, C_1 - C_{10} alkyl, C_3 - C_{10} cycloalkyl, C_6 - C_{14} aryl, C_3 - C_{13} heteroaryl, C_7 - C_{24} alkaryl, C_4 - C_{23} alkheteroaryl, up to perhalosubstituted C_1 - C_{10} alkyl, up to perhalosubstituted C_3 - C_{10} cycloalkyl, up to perhalosubstituted C_3 - C_{13} heteroaryl; and

wherein R^4 and $R^{4'}$ are independently selected from the group consisting of H, C_1 - C_{10} alkyl, C_3 - C_{10} cycloalkyl, C_6 - C_{14} aryl, C_3 - C_{13} heteroaryl; C_7 - C_{24} alkaryl, C_4 - C_{23} alkheteroaryl, up to per-halosubstituted C_1 - C_{10} alkyl, up to per-halosubstituted C_3 - C_{10} cycloalkyl, up to per-halosubstituted C_6 - C_{14} aryl and up to per-halosubstituted C_3 - C_{13} heteroaryl,

 R^a is C_1 - C_{10} alkyl, C_3 - C_{10} cycloalkyl, up to per-halosubstituted C_1 - C_{10} alkyl and up to per-halosubstituted C_3 - C_{10} cycloalkyl; and

R^b is hydrogen or halogen,

 R^c is hydrogen, halogen, C_1 - C_{10} alkyl, up to per-halosubstituted C_1 - C_{10} alkyl or combines with R^1 and the ring carbon atoms to which R^1 and R^c are bound to form a 5- or 6-membered cycloalkyl, aryl or hetaryl ring with 0-2 members selected from O, N and S

3. (Amended) A method of claim 1, wherein B is

DO

$$X_n$$
 $Q - (Y - Q^1)_s Z_{n1}$

wherein Y is selected from the group consisting of -O-, -S-, -CH₂-, -SCH₂-, -CH₂S-, -CH(OH)-, -C(O)-, -CX^a₂, -CX^aH-, -CH₂O- and -OCH₂-, where X^a is halogen,

Q is a six member aromatic structure containing 0-2 nitrogen, substituted or unsubstituted by halogen, up to per-halosubstitution;

Q¹ is a mono- or bicyclic aromatic structure of 3 to 10 carbon atoms and 0-4 members of the group consisting of N, O and S, unsubstituted or unsubstituted by halogen up to per-halosubstitution, and

X, Z, n and n1 are as defined in claim 1 and s is 0 or 1.

6. (Amended) A method as in claim 5, wherein B is 2,3-dichlorophenyl or of the formula



$$X_n$$
 $Q - (Y - Q^1)_s - Z_{n1}$

wherein Q is phenyl, Q^1 is phenyl or pyridinyl, Y is -O-, -S-, -CH₂- or -SCH₂, X is CF₃, and Z is -OH, -Cl or NHC(O)-C_pH_{2p+1}, where p = 2-4, s = 0 or 1, n = 0 and n1 = 0 or 1.

14. (Amended) A method as in claim 13, wherein B is 2,3-dichlorophenyl or of the formula



$$-Q^{1}$$

wherein Q is phenyl, Q^1 is phenyl, pyridinyl or benzothiazolyl, Y is -O-, -S-, $-CH_2$ - or -NH-, Z is Cl, $-CH_3$ or $-OCH_3$, s=0 or 1, n=0 and n1=0 or 1.



- 28. (Amended) A method as in claim 1, wherein the compound for formula I displays p38 IC $_{50}$'s of less than 10 μ m as determined by an in-vitro p38 kinase inhibition assay.
- **29.** (Amended) A method according to claim 1, wherein the disease is mediated by a cytokine and/or protease (proteolytic enzyme) regulated by p38.



31. (Amended)A method according to claim 29, comprising administering an amount of a compound of formula I effective to inhibit production of a disease-mediating cytokine or protease.

-42. (New) A method for the treatment of cancerous cell growth mediated by raf kinase

comprising administering a compound of formula !

O || A-NH-C-NH-B

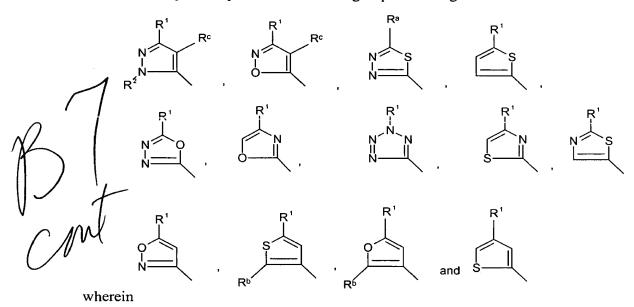
wherein B is phenyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, naphthyl, quinolinyl, isoquinolinyl, phthalimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzofuryl, benzothienyl, indolyl, benzopyrazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl or benzisothiazolyl, substituted by one or more substituents independently selected from the group consisting of halogen, up to perhalosubstitution, and X_n, wherein n is 0-3 and each X is independently selected from the group consisting of -CN, $-CO_2R^5$, $-C(O)NR^5R^{5'}$, $-C(O)R^5$, $-NO_2$, $-OR^5$, $-SR^5$, $-NR^5R^{5'}$, - $NR^5C(O)OR^{5'}$, $-NR^5C(O)R^{5'}$, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_1-C_{10} alkoxy, C_3-C_{10} cycloalkyl, phenyl, pyridinyl, naphthyl, isoquinolinyl, quinolinyl up to per halosubstituted C₁-C₁₀ alkyl, up to per halo-substituted C₂-C₁₀ alkenyl, up to per halosubstituted C₁-C₁₀ alkoxy, up to per halo-substituted C₃-C₁₀ cycloalkyl, and -Y-Ar;

wherein R⁵ and R⁵ are independently selected from H, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₃-C₁₀ cycloalkyl, up to per-halosubstituted C₁-C₁₀ alkyl, up to perhalosubstituted C₂-C₁₀ alkenyl, and up to per-halosubstituted C₃-C₁₀ cycloalkyl,

wherein Y is - O-, -S-, -N(\mathbb{R}^5)-, -(CH₂)-_m, -C(O)-, -CH(OH)-, -(CH₂)_mO-, $-NR^5C(O)NR^5NR^{5'}$ -, $-NR^5C(O)$ -, $-C(O)NR^5$ -, $-(CH_2)_mS$ -, $-(CH_2)_mN(R^5)$ -, $-O(CH_2)_m$ -, -CHX^a, -CX^a₂-, -S-(CH₂)_m- and -N(R⁵)(CH₂)_m-,

m=1/3, and X^a is halogen; and Ar is phenyl, pyridinyl, pyrimidinyl, pyridazinyl, naphthyl, quinolinyl, isoquinolinyl, phthalimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzofuryl, benzothienyl, indolyl, benzopyrazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl or benzisothiazolyl, optionally substituted by halogen up to per-halosubstitution and optionally substituted by Z_{n1} , wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, =O, -CO₂R⁵, -

 $C(O)NR^5R^5'$, $-C(O)-NR^5$, $-NO_2$, $-OR^5$, $-SR^5$, $-NR^5R^5'$, $-NR^5C(O)OR^5'$, $-C(O)R^5$, $-NR^5C(O)R^5'$, $-SO_2R^5$, $SO_2NR^5R^5'$, C_1-C_{10} alkyl, C_1-C_{10} alkoxyl, C_3-C_{10} cycloalkyl, up to per halo-substituted C_1-C_{10} alkyl, and up to per halo-substituted C_3-C_{10} cycloalkyl, and A is a heteroaryl moiety selected from the group consisting of



 R^{1} is selected from the group consisting of halogen, C_{3} - C_{10} alkyl, C_{3} - C_{10} cycloalkyl, C_{1} - C_{13} heteroaryl, C_{6} - $_{14}$ aryl, C_{7} - $_{24}$ alkaryl, up to per-halosubstituted C_{1} - C_{10} alkyl, up to per-halosubstituted C_{3} - C_{10} cycloalkyl, up to per-halosubstituted C_{1} - C_{13} heteroaryl, up to per-halosubstituted C_{6} - $_{14}$ aryl, and up to per-halosubstituted C_{7} - $_{24}$ alkaryl;

 R^2 is selected from the group consisting of H, $-C(O)R^4$, $-CO_2R^4$, $-C(O)NR^3R^{3'}$, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_7-C_{24} alkaryl, C_4-C_{23} alkheteroaryl, substituted C_1-C_{10} alkyl, substituted C_3-C_{10} cycloalkyl, substituted C_7-C_{24} alkaryl and substituted C_4-C_{23} alkheteroaryl,

where R^2 is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of -CN, - CO_2R^4 , -C(O)-NR³R^{3'}, -NO₂, -OR⁴, -SR⁴, and halogen up to per-halosubstitution,

wherein R^3 and $R^{3'}$ are independently selected from the group consisting of H, - OR^4 , - SR^4 , - $NR^4R^{4'}$, - $C(O)R^4$, - CO_2R^4 , - $C(O)NR^4R^{4'}$, C_1 - C_{10} alkyl, C_3 - C_{10} cycloalkyl, phenyl, pyridinyl, naphthyl, isoquinolinyl or quinolinyl

up to per-halosubstituted C_1 - C_{10} alkyl, up to per-halosubstituted C_3 - C_{10} cycloalkyl, and up to per-halosubstituted, phenyl, pyridinyl, naphthyl, isoquinolinyl or quinolinyl and

wherein R^4 and R^4 are independently selected from the group consisting of H, C_{1-} C_{10} alkyl, C_3 - C_{10} cycloalkyl, , phenyl, pyridinyl, naphthyl, isoquinolinyl, quinolinyl up to per-halosubstituted C_1 - C_{10} alkyl, up to per-halosubstituted C_3 - C_{10} cycloalkyl, and up to per-halosubstituted, phenyl, pyridinyl, naphthyl, isoquinolinyl or quinolinyl,

 R^a is C_1 - C_{10} alkyl, C_3 - C_{10} cycloalkyl, up to per-halosubstituted C_1 - C_{10} alkyl and up to per-halosubstituted C_3 - C_{10} cycloalkyl; and

R^b is hydrogen or halogen,

 R^c is hydrogen, halogen, C_1 - C_{10} alkyl, up to per-halosubstituted C_1 - C_{10} alkyl or combines with R^1 and the ring carbon atoms to which R^1 and R^c are bound to form a 5- or 6-membered cycloalkyl, aryl or hetaryl ring with 0-2 members selected from O, N and S.

43. (New) A method as in claim 42, wherein B is

$$- \bigvee_{\text{or}} X_n - \bigvee_{\text{or}} X_n$$

which is substituted or unsubstituted by halogen, up to per-halosubstitution, and wherein

$$n = 1-3$$
 and

each X is independently selected from the group consisting of C_{1-4} alkyl, up to perhalosubstituted C_{1-4} alkyl and -Y-Ar;

wherein Y is - O-, -S-, -N(
$$R^5$$
)-, -(CH₂)-_m, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -NR⁵C(O)NR⁵ NR^{5'}-, -NR⁵C(O)-, -C(O)NR⁵-, -(CH₂)_mS-, -(CH₂)_mN(R^5)-, -O(CH₂)_m-, -CHX^a, -CX^a₂-, -S-(CH₂)_m- and -N(R^5)(CH₂)_m-,

m = 1-3, and X^a is halogen; and

Ar is phenyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, naphthyl, quinolinyl, isoquinolinyl, phthalimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzofuryl, benzothienyl, indolyl, benzopyrazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl or benzisothiazolyl, optionally substituted by halogen up to per-halosubstitution and optionally substituted by Z_{n1} , wherein nl is 0 to 3 and each Z is independently selected from the group consisting of -CN, =O,

-CO₂R⁵, -C(O)NR⁵R⁵, -C(O)R⁵, -NO₂, -OR⁵, -SR⁵, -NR⁵R⁵, -NR⁵C(O)OR⁵, -C(O)R⁵, -NR⁵C(O)R⁵, -SO₂R⁵, -SO₂R⁵R⁵, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, C₃-C₁₀ cycloalkyl, up to per halo-substituted C₁-C₁₀ alkyl, and up to per halo-substituted C₃-C₁₀ cycloalkyl, wherein R⁵ and R⁵ are independently selected from H, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₃-C₁₀ cycloalkyl, up to per-halosubstituted C₁-C₁₀ alkyl, up to per-halosubstituted C₂-C₁₀ alkenyl and up to per-halosubstituted C₃-C₁₀ cycloalkyl.

44. (New) A method as in claim 5, wherein B is of the formula

$$-Q^{-}$$
 $(Y-Q^{1})_{s}$ Z_{n1}

wherein Q is phenyl or pyridinyl, optionally substituted by halogen up to perhalosubstitution, Q^1 is pyridinyl, phenyl or benzothiazolyl optionally substituted by halogen up to per-halosubstitution, Y is -O-, -S-, -CH₂S-, -SCH₂-, -CH₂O-, -OCH₂- or - CH₂-, X is C₁-C₄ alkyl or up to per-halosubstituted C₁-C₄ alkyl and Z is as defined in claim 1, n = 0 or 1, s = 1 and n1 = 0-1.

45. (New) A method as in claim 9, wherein B is of the formula

Q is phenyl or pyridinyl, optionally substituted by halogen up to per-halosubstitution, Q^1 is pyridinyl, phenyl or benzothiazolyl optionally substituted by halogen up to per-halosubstitution, Y is -O-, -S-, -C(O)- or $-CH_2$ -, X is C_1 - C_4 alkyl or up to per-halosubstituted C_1 - C_4 alkyl and Z is as defined in claim 1 n = 0 or 1, s = 0 or 1 and n1 = 0 or 1.

46. (New) A method as in claim 13, wherein B is of the formula

$$-Q - \left(Y - Q^{1}\right)_{c} Z_{n1}$$

Q is phenyl or pyridinyl optionally substituted by halogen up to per-halosubstitution, Q^1 is phenyl, benzothiazolyl or pyridinyl optionally substituted by halogen up to per-halosubstitution, Y is -O-, -S- or $-CH_2$ -, X is C_1 - C_4 alkyl or up to per-halosubstituted C_1 - C_4 alkyl, Z is as defined in claim 1, n = 0 or 1, s = 1, and n1 = 0 or 1.

47. (New) A method as in claim 17, wherein B is of the formula

$$X_n$$
 Q — $(Y$ — $Q^1)_s$ — Z_{n1}

wherein Q is phenyl optionally substituted by halogen up to per-halosubstitution, Q^1 is phenyl or pyridinyl optionally substituted by halogen up to per-halosubstitution, Y is -O-or -S-, X is C_1 - C_4 alkyl or up to per-halosubstituted C_1 - C_4 alkyl, Z is as defined in claim 1, n = 0 or 1, s = 0 or 1 and n1 = 0-2.

48. (New) A method as in claim 22, wherein B is of the formula

$$-Q^{-}$$
 $(Y^{-}Q^{1})_{s}$ Z_{n1}

wherein Q is phenyl optionally substituted by halogen up to per-halosubstitution, Q^1 is phenyl or pyridinyl optionally substituted by halogen up to per-halosubstitution, Y is -O-or -S-, X is C_1 - C_4 alkyl or up to per-halosubstituted C_1 - C_4 alkyl, s=1, Z is as defined in claim 1, n=0 or 1 and n1=0 or 1.

49. (New) A method as in claim 28, wherein B is of the formula

$$-Q^{-}(Y-Q^{1})_{s}^{-}Z_{n1}$$

wherein Q is phenyl optionally substituted by halogen up to per-halosubstitution, Q^1 is phenyl or pyridinyl optionally substituted by halogen up to per-halosubstitution, and Y is $Q^1 - Q^2 - Q^$

50. (New) A method as in claim 1, wherein B is

a) phenyl, pyridinyl, naphthyl, quinolinyl or isoquinolinyl, substituted by -Y-Ar and optionally substituted by

- -halogen up to per-halosubstitution,
- -C₁-C₄ alkyl,
- -up to per-halosubstituted C₁-C₄ alkyl, or
- a combination thereof,

wherein Y and Ar are as defined in claim 1;

- b) thienyl substituted by methyl; or
- c) indolyl substituted by phenyl or pyridyl.

51. (NEW) A method as in claim 1, wherein B is phenyl or pyridinyl substituted by -Y-Ar and optionally substituted by

- -halogen ,up to per-halosubstitution,
- -C₁-C₄ alkyl,
- -up to per-halosubstituted C₁-C₄ alkyl, or
- a combination thereof,

wherein Y and Ar are as defined in claim 1.

52. (NEW) A compound of one of the formulae

a)



wherein R⁶ is -O-CH₂-phenyl, -NH-C(O)-O-t-butyl, -O-n-pentyl, -O-n-butyl, -C(O)-N(CH₃)₂ , -O-CH₂CH(CH₃)₂ or -O-n-propyl,

c)

wherein R¹ is -CH₂-t-butyl;

d)

wherein R^2 is $-CH_2CF_3$, $-C_2H_4$ -OH, $-CH_2$ -(3-HOC₆H₄), $-CH_2C(O)NHCH_3$, -CH₂C(O)OC₂H₅, -C₂H₄CN, or

or

h)

and pharmaceutically acceptable salts thereof.

53. (NEW) A pharmaceutical composition comprising a compound according to claim 52 or a pharmaceutically acceptable salt thereof and a physiologically acceptable carrier.--